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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/472,691	12/27/99	HERMISTON T	ONYX1022

HM22/0517
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EXAMINER	
SORRELL O.F	
ART UNIT	**PAPER NUMBER**
1633	4

DATE MAILED: 05/17/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

file copy

Office Action Summary	Application No.	Applicant(s)	
	09/472,691	HERMISTON ET AL.	
	Examiner	Art Unit	
	Eleanor Sorbello	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☒ Other: *See Continuation Sheet* .

Continuation of 19. Other: Notice to comply with sequence requirements.

DETAILED ACTION

Priority

1. It is acknowledged that this application claims priority to two U.S. Provisional Applications.

(a) Application No. 60/117,814 filed January 28, 1999.

(b) Application No. 60/157,288 filed October 1, 1999.

Claims

2. Claims 1-12 are pending in this application.

Sequence Compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant must comply with the sequence rules, 37 CFR 1.821 - 1.825 in response to this office action. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

5. Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for therapy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant invention claims methods of treating mammals with neoplastic conditions comprising administering the adenoviral constructs in therapeutically effective dosages. The specification while being enabled for the construction of adenoviral E1B shuttle vectors comprising deletions of the entire E1B region or one or more genes in this region, does not teach one how this could be used to provide gene therapy.

The state of the art in gene therapy is still in its infancy and is highly unpredictable. "Clinical efficacy has not been definitely demonstrated at this time in any gene therapy protocol" (see Orkin et al. Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy, distributed by the National Institutes of Health, Bethesda, MD or www. nih.gov, page 1).

Gene therapy aims to alleviate or cure diseases by altering the genetic makeup of the individual. The first clinical trials for genetic therapy were conducted in 1990. However, there is still no single outcome to point to as a success story after hundreds of clinical trials have been performed worldwide on thousands of individuals. (See Verma, M. et al., Gene Therapy-promises, problems and prospects, Nature Vol. 389 page 239, paragraph # 2). The major problems that have been encountered are (1) the delivery of the altered genes, and (2) the inability to obtain a sustained expression of the desired protein in a specified location. (See Verma, M. et al., Gene Therapy-promises, problems and prospects, Nature Vol. 389 page 239, paragraph # 5).

Being a new field the amount of direction or guidance necessary in the specification has to be very detailed in order to provide enablement. In this case, the state of the prior art does not teach one skilled in the art how to transfer a gene and induce a therapeutic response. Hence the specification requires detailed methods for preparation of the therapeutic compositions comprising the adenoviral vector with specific dosages for specific therapies as claimed by the inventions. This is made clear by the MPEP 608.01(p) where it states: "If the use disclosed is of such nature that the art is unaware of successful treatments with chemically analogous compounds, a more complete statement of how to use must be supplied...".

The specification describes the preparation of a recombinant adenoviral vector containing transgenes inserted where the E1B genes were deleted, but does not teach how these are to be used for therapy. The specification however contains prophetic

statements that the said vector could be used for therapy. No working examples have been provided.

In view of this, it would prove an arduous task for one skilled in the art to be able to practice the claimed invention of gene therapy. Hence, since one skilled in the art cannot readily anticipate the results predicted within the subject matter to which the claimed invention pertains, then there is a lack of predictability in the art.

In conclusion, given the nature of the invention, the state of the art, the demonstrated lack of predictability of the art, the amount of guidance set forth, the breadth of the claims, and the lack of working examples, one of skill in the art could not make and use the invention without undue experimentation.

6. Claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an adenoviral vector in cells that are isolated or cultured, does not reasonably provide enablement for cells transfected with the adenoviral vector in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

For reasons discussed above, the specification does not enable one of skill in the art to make or use cells transfected in vivo.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 1, uses the term 'substantially', and is rejected as being unclear. One of skill in the art is not reasonably apprised of how substantial or to what extent the expression of the transgene inserted into the applicant's vector is expected to be, unless it is explicitly stated. Hence the claim should be amended. Claims depeding upon Claim 1 are rejected for the same reason.

Claim 1, uses the term 'optionally', and is rejected as being unclear. It is not clear to one skilled in the art as to what function the vector would have if it did not have a heterologous gene inserted into it. As the term is unclear, it could also be taken to mean that another gene having the function of the E1B region is substituted for it. Therefore the claim should be amended to clearly state the intended meaning. Claims depending upon Claim 1 are rejected for the same reason.

Claim 5 and 12 uses the phrase " vector that has the properties of a recombinant adenoviral vector consisting of", which is vague and indefinite. It is not evident to one of skill in the art, as to what properties the vector is supposed to have. The claim should be amended to reflect the specific properties intended in the invention. Otherwise the skilled artisan is not reasonably apprised as to the metes and bounds of the claims.

9. Claims 3 and 4 do not further limit claim 2. It appears applicants intended the genes to be written in the alternative. The claims have been examined as such.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claims 1- 4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hung et al. (patent # 5,643,567).

Claim 1, is directed to a recombinant adenoviral vector comprising a deletion of genes in the E1B region, and claims 2-4 are directed to specific deletions within the E1B region.

Hung et al. taught a recombinant adenoviral vector comprising a deletion in the E1B region could be used as a gene delivery system. (See column 49, lines 20-34). They inserted the E1A gene, which can be considered to be a tumor suppressor gene, or its structural homologue the LT gene, having a similar function, in place of the deleted E1B region. (See abstract, and column 2, lines 63-67).

12. Claims 1,2,4-9, and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Gregory et al. (patent No. 5,932,210).

Claim 4 is directed to an adenoviral vector comprising a deletion in the pIX gene of the E1B region.

Gregory et al. constructed recombinant adenoviral expression vectors characterized by a total or partial deletion of the pIX gene located within the E1B region. (See Abstract).

Claim 6 is directed to an adenoviral vector comprising a deletion in the E1B region where a heterologous gene encoding a cell suicide gene is inserted.

Claim 6 is rejected as Gregory et al. taught that this adenoviral vector can contain a suicide gene (see Abstract) or a conditional suicide gene encoding thymidine kinase.

Claim 5, is directed to an adenoviral vector, and claim 12 isdirected to a replication competent recombinant adenoviral vector (with the E1B deletion), that has properties conferred to it by virtue of the cytosine deaminase (CD) gene inserted in place of the E1B region.

Claims 5 and 12 are rejected as Gregory et al. taught the construction of a replication competent recombinant adenovirus with the E1B region deleted and a gene expressing cytosine deaminase inserted in it which shares properties with pΔE1B/CD. (See column 13, lines 39-65).

Claims 7-9 are directed to cells comprising the adenoviral vectors comprising the deletion of genes within the E1B region.

Claims 7-9 are rejected by Gregory et al. as they taught the transformation of host cells by the recombinant adenoviral vectors with a total deletion of the E1B DNA.(See Abstract, line 5).

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DEBORAH J. CLARK
PATENT EXAMINER